

## Thyroid cancer and employment as a radiologic technologist

Erik W. Zabel<sup>1</sup>, Bruce H. Alexander<sup>1\*</sup>, Steven J. Mongin<sup>1</sup>, Michele M. Doody<sup>2</sup>, Alice J. Sigurdson<sup>2</sup>, Martha S. Linet<sup>2</sup>, D. Michal Freedman<sup>2</sup>, Michael Hauptmann<sup>3</sup>, Kiyohiko Mabuchi<sup>2</sup> and Elaine Ron<sup>2</sup>

<sup>1</sup>Division of Environmental Health Sciences, School of Public Health, University of Minnesota, Minneapolis, MN

<sup>2</sup>Radiation Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute,

NIH, DHHS, Bethesda, MD

<sup>3</sup>Biostatistics Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, DHHS, Bethesda, MD

The association between chronic occupational ionizing radiation exposure in the medical field and thyroid cancer is not well characterized. Thyroid cancer incidence was ascertained for 2 periods in a cohort of radiologic technologists certified for a minimum 2 years and enumerated in 1983: (i) cases identified prospectively in 73,080 radiologic technologists who were free of thyroid cancer at the baseline survey and completed a second questionnaire a decade later ( $N = 121$ ), and (ii) cases occurring prior to cohort enumeration among 90,245 technologists who completed the baseline survey and were thyroid cancer free 2 years after certification ( $N = 148$ ). Survival analyses estimated risks associated with employment as a radiologic technologist, including duration of employment, period of employment, types of procedures and work practices. The only occupational history characteristic associated with prospectively identified thyroid cancer was a history of holding patients for X-ray procedures at least 50 times ( $HR = 1.47$ , 95%  $CI = 1.01$ – $2.15$ ). Total years worked as a radiologic technologist, years performing diagnostic, therapeutic, and nuclear medicine procedures, employment under age 20 and calendar period of first employment were not associated with thyroid cancer risk. Risk of thyroid cancers diagnosed before the baseline questionnaire was inversely associated with decade first employed as a technologist, and was elevated, albeit imprecisely, among those working more than 5 years prior to 1950 ( $HR = 3.04$ , 95%  $CI = 1.01$ – $10.78$ ). These data provide modest evidence of an association between employment as a radiologic technologist and thyroid cancer risk; however, the findings require confirmation with more accurate exposure models.

© 2006 Wiley-Liss, Inc.

**Key words:** ionizing radiation; thyroid cancer; occupational exposure; epidemiology

Malignant neoplasms of the thyroid, although relatively rare, are increasing in the United States and other developed countries at a higher rate than most other cancers.<sup>1,2</sup> Female sex, a history of benign thyroid disease and ionizing radiation are established risk factors for thyroid cancer,<sup>3,4</sup> however the risk associated with ionizing radiation exposure in adulthood is not clear. Thyroid cancer incidence over time correlates with the common use of radiation treatment for benign neck and head conditions between 1930 and 1960.<sup>5</sup> Children and adolescents with single exposure to a wide range of doses following the atomic bombings in Hiroshima and Nagasaki had elevated rates of thyroid cancer, but there was little evidence for an increased risk when exposure occurred as an adult ( $>20$  years old).<sup>6</sup> Studies of people living near the Chernobyl accident site suggest large thyroid cancer risks among persons exposed as children, but risks following adult exposure are uncertain.<sup>7,8</sup>

Occupational exposure to ionizing radiation is common in the medical field, as well as in mining operations and the nuclear power industry. These exposures are characterized by chronic low-dose fractions over many years during a working lifetime. Studies of thyroid cancer and occupational ionizing radiation exposure have mainly evaluated mortality as the outcome; however, the relatively high survival for thyroid cancer makes the interpretation of these data problematic. Results from occupational studies that evaluated thyroid cancer incidence provide inconsistent evidence. Radiation exposed workers in Canada had a modest excess risk of thyroid cancer incidence compared to the general population; however, no excess was observed when the rates were compared by levels of ex-

posure within the cohort.<sup>9</sup> Chinese medical X-ray workers were reported to have an excess of incident thyroid cancer compared to other medical workers; however, this finding was based on few cases.<sup>10</sup> A previous analysis of cancer incidence in the U.S. radiologic technologists cohort, the population on which we report here, revealed a modest excess risk of thyroid cancer incidence compared to that expected based on the US population.<sup>11</sup> To date the investigations of occupational ionizing radiation exposure and thyroid cancer risk has relied on relatively broad occupational classifications as exposure metrics.<sup>9,10,12,13</sup> A more detailed evaluation of determinants of occupational radiation exposure in the medical field and thyroid cancer has not been done.

To determine whether occupational radiation exposure associated with employment as a radiologic technologist is related to the risk of thyroid cancer, we evaluated the incidence of thyroid cancer in a cohort of registered radiologic technologists.

### Methods

The United States Radiologic Technologists (USRT) cohort includes all registered radiologic technologists certified for a minimum of 2 years by the American Registry of Radiologic Technologists ( $N = 146,022$ ) as of 1982. Information pertaining to demographics, lifestyle, work history, medical history, including the occurrence of cancer was collected with 2 postal questionnaires. The details of the questionnaire design and study protocol have been reported previously.<sup>14,15</sup> Briefly, the cohort was enumerated and a baseline questionnaire was mailed in 1983 through 1984 to 132,519 technologists known to be alive and for whom an address was available. A total of 90,305 responded and returned the questionnaire between 1983 and 1990. A second questionnaire was mailed to 125,707 living technologists beginning in 1994, of whom 91,173 responded by August 1998. Both questionnaires were completed and returned by 70,859 technologists. Mortality and underlying and contributing cause of death were determined using vital records.

Evaluating the association between occupational exposure to ionizing radiation and prospectively identified incident thyroid cancer was the primary focus of this analysis. Technologists who were thyroid cancer free upon completion of the first survey and also responded to the second survey or died before the second survey period was completed in August 1998 ( $N = 2,415$ ) are included in the analysis ( $N = 73,080$ ). Follow-up of the cohort members was conducted from the date of first questionnaire completion until the diagnosis of thyroid cancer, death or completion

Erik W. Zabel's current address is: Division of Environmental Health, Minnesota Department of Health, St. Paul, MN, USA.

Grant sponsor: Division of Cancer Epidemiology and Genetics, Department of Health and Human Services, National Cancer Institute, National Institutes of Health.

\*Correspondence to: Dr. Bruce Alexander, Division of Environmental Health Sciences, School of Public Health, University of Minnesota, MMC 807, Mayo Building, 420 Delaware Street S.E., Minneapolis, MN 55455, USA. Fax: +612-626-483. E-mail: balex@umn.edu

Received 5 October 2005; Accepted 2 March 2006

DOI 10.1002/ijc.22065

Published online 30 May 2006 in Wiley InterScience (www.interscience.wiley.com).

of the second questionnaire. Thyroid cancer cases were ascertained through self-reporting on mailed questionnaires and reported as a cause of death on death certificates. By including thyroid cancers identified on the death certificate we assume the following: (i) the initial diagnosis was made after the first questionnaire was completed, and (ii) that thyroid cancer is rare enough that decedents with no mention of thyroid cancer on the death certificate were never diagnosed with thyroid cancer. Participants with a diagnosis of thyroid cancer before the first questionnaire completion date were excluded from the prospective analysis, but were evaluated in a separate retrospective analysis (described later). Living participants reporting thyroid cancer were contacted to obtain consent to acquire medical records to validate the diagnosis. If information obtained from the participant or physician of record during the validation process indicated the reported diagnosis was incorrect the case was reclassified as a noncase. If the participant declined to release medical records, or the physician of record was not able to locate the records, the case was included in the analysis as a thyroid cancer.

Work history data collected on the first questionnaire were used as surrogate measures of occupational exposure to ionizing radiation. Years worked as a radiologic technologist formed the primary basis for the exposure assessment. The eras first worked as a radiologic technologist, before 1960, 1960 through 1969 and 1970 or later, were included in the exposure analysis to account for secular changes in occupational ionizing radiation exposure. The levels of exposure have declined over time because of engineering changes in the equipment and workplace, and greater adherence to personal protective practices. Estimates for changes over time suggest that exposures prior to the 1960s were 5 to more than 20 times greater than after 1960.<sup>16</sup> Because exposure at a younger age is an important determinant for developing radiation related thyroid cancer, the effects of working as a radiologic technologist before age 20 were examined. In addition to the years of work as a radiologic technologist, the amounts of time spent performing specific procedures were evaluated as surrogate exposure metrics. The number of years working with diagnostic procedures (fluoroscopy, dental, routine X-ray, multifilm and CAT scan), therapeutic procedures (orthovoltage, cobalt 60, betatron and other X-ray teletherapy), and nuclear medicine procedures (diagnostic radioisotopes, radium therapy and other radioisotope therapy) were evaluated as total years worked and by era first worked. The self-reported practice of holding patients for X-rays, which places the technologist close to the exposure source, and having X-rays practiced on oneself were also evaluated as surrogates of radiation exposure. The potentially confounding effects of age, gender, body mass index (BMI), smoking habit, history of benign thyroid conditions, X-ray treatment of the head and neck and age at menarche and parity among female technologists were examined.

Cox proportional hazards models were used to estimate hazard ratios (HR) for occupational and nonoccupational characteristics ascertained at baseline while examining the effect of, and adjusting for potentially confounding variables.<sup>17</sup> To allow for flexibility to handle effects that may vary over time, piece-wise constant hazard models were also used to estimate HRs, while adjusting for baseline covariates of age and sex.<sup>18</sup> In this model, the 14-year follow-up period was divided into 4 equal sized intervals and a HR was estimated for each of the 4 intervals. A summary HR, which can be interpreted as an average of the separate HRs, was estimated for the entire follow-up period. The study time origin, at which the baseline characteristics of the cohort were established, was taken as the earliest date of mailing of the first questionnaire (June 1983). Participants contributed person-time at risk from completion of the first questionnaire until date of diagnosis of thyroid cancer, date of death or the date of completion of the second questionnaire. The precision of the HRs is described with 95% confidence intervals.

A separate analysis evaluated the risk of thyroid cancer diagnosed before the administration of the first questionnaire, among all technologists responding to the first questionnaire ( $N = 90,245$ ) who were thyroid cancer free when they became eligible

for inclusion in the cohort (2 years postcertification). This analysis is presented separately because the population includes all respondents to the first questionnaire and all information on potential risk factors, including work history, was obtained after the diagnosis of thyroid cancer. This analysis focused on employment characteristics that could be reasonably assigned prior to onset of thyroid cancer. HRs were estimated with proportional hazards models<sup>17</sup> using age as the metric of person-time beginning with the age of eligibility (certified for 2 years) until diagnosis of thyroid cancer or completion of the first questionnaire. The risk of thyroid cancer was evaluated by duration of employment, era of employment, age at first employment and selected work practices that may increase exposure, specifically routine use of lead apron when first working and number of times patients were held for procedures. The categories for the year first worked and the number of times patients were held differed from the prospective analysis as the practices and eras worked differed for the thyroid cancer cases diagnosed in earlier years. Models were adjusted for sex, birth cohort and work history variables potentially associated with exposure and the risk and diagnosis of thyroid cancer.

## Results

### *Prospectively identified thyroid cancer*

The initial case ascertainment identified 134 incident thyroid cancers. Of these, 13 were determined not to be eligible. Nine were found not to be thyroid cancer through follow-up with the participant or based on medical records, 1 case had a diagnosis date prior to the completion of the first questionnaire and 3 cancers were reported to the study office after completion of the second questionnaire and thus outside the ascertainment period. Ultimately 121 cases of thyroid cancer were included in the prospective incidence analysis. The diagnosis of thyroid cancer was positively confirmed with medical records for 100 of these cases (82.6%), and of the reported cases for which some validation information was obtained, the positive predictive value was 91.7%. Papillary carcinoma was the major histological type in the confirmed cases (83%). The average age at diagnosis was 43 and ranged from 27 to 68.

Men were less likely to develop thyroid cancer compared to women (HR = 0.57, 95% CI = 0.33–0.98) (Table I). A higher BMI was associated with an increased risk of thyroid cancer with HRs for the middle and top tertiles compared to the lowest of 1.53 (95% CI = 0.95–2.48) and 1.79 (95% CI = 1.04–2.95), respectively. Smokers had a modestly lower risk of developing thyroid cancer (HR = 0.79, 95% CI = 0.51–1.45). A reported history of any X-ray therapy to the head and neck was positively associated with thyroid cancer risk with a HR of 4.16 (95% CI = 2.01–8.63). Twenty-seven of the thyroid cancer cases had a prior diagnosis of at least one previous benign thyroid condition, which corresponded to a HR of 3.06 (95% CI = 1.96–4.77). A history of X-ray therapy and benign thyroid conditions were clearly predictors of thyroid cancer risk but were unrelated to occupational exposures and were, therefore, not included in the final models.

The risk of thyroid cancer did not increase with the total number of years worked as a radiologic technologist (Table II). Era of first employment did not influence the risk of thyroid cancer, but the duration of employment before 1960 was positively, albeit imprecisely, associated with thyroid cancer. Age of first employment was not associated with thyroid cancer incidence (Table II).

Technologists who reported holding patients for X-rays 50 or more times had an elevated risk of thyroid cancer (HR = 1.47, 95% CI = 1.01–2.15) and those who had X-rays practiced on themselves had an increased risk of similar magnitude but with a wide confidence interval (HR = 1.46; 0.86–2.46) (Table III). The types of procedures did not appear to influence thyroid cancer risk. A modest but imprecise elevation in risk was associated with working with diagnostic procedures in the pre 1960 era. Beginning work under age 20 and holding patients for procedures varied slightly across eras of first employment (Table IV). Higher occupational radiation exposures would be expected before the 1960s compared to later.

**TABLE 1** – CHARACTERISTICS OF PARTICIPANTS IN THE US RADIOLOGIC TECHNOLOGISTS STUDY WITH THYROID CANCER DIAGNOSED DURING THE FIRST FOLLOW-UP PERIOD (1983–1998), FREE OF THYROID CANCER AND WITH THYROID CANCER DIAGNOSED 2 YEARS POSTCERTIFICATION, BUT PRIOR TO BASELINE QUESTIONNAIRE

	Thyroid cancer after baseline <sup>1</sup>		Thyroid cancer free <sup>1</sup>		Thyroid cancer before baseline <sup>2</sup>	
	N	%	N	%	N	%
Gender						
Female	104	86.0	56,906	78.0	127	85.8
Male	17	14.0	16,053	22.0	21	14.2
Age at baseline						
≤30	34	28.1	20,690	28.4	18	12.2
31–40	57	47.1	30,225	41.4	57	38.5
41–50	22	18.2	13,484	18.5	37	25.0
≥51	8	6.6	8,560	11.8	36	24.3
Age first worked						
<18	1	0.8	1,383	1.9	6	4.1
18–20	78	64.5	42,577	58.4	79	53.4
≥21	41	33.9	27,260	37.4	60	40.5
Unknown or did not work	1	0.8	1,739	2.4	3	2.0
Year first worked						
≥1970	59	48.8	34,068	46.7	32	21.6
1960–1969	42	34.7	22,798	31.2	51	34.5
1950–1959	16	13.2	10,574	14.5	36	24.3
1940–1949	3	2.5	3,611	4.9	20	13.5
<1940	0	0.0	813	1.1	6	4.1
Unknown or did not work	1	0.8	1,095	1.5	3	2.0
Ethnic group						
White	118	97.5	68,564	94.0	138	93.2
Non-white	3	2.5	3,702	5.1	10	6.4
Other	0	0	693	0.9	0	0.0
Body mass index (kg/m <sup>2</sup> ) tertiles						
<21.5	32	26.5	23,886	32.7	46	31.1
21.5–24.4	39	32.2	23,106	31.7	45	30.4
>24.4	45	37.2	23,400	32.1	50	33.8
Missing	5	4.1	2,567	3.5	7	4.7
Ever smoked 100 cigarettes	55	45.5	37,947	52.0	63	42.6
Prior thyroid condition	27	22.3	6,589	9.0	NA <sup>3</sup>	NA
Therapeutic X-ray of head	9	7.4	1,443	2.0	12	8.1
Age at Menarche <sup>4</sup>						
≤12	66	63.5	26,967	47.4	52	40.9
≥13	36	34.6	29,093	51.1	72	56.7
Missing	2	1.9	846	1.5	3	2.4
Number of live births <sup>4</sup>						
0	22	21.2	17,178	30.2	4	3.2
≥1	76	73.1	37,094	65.2	86	67.6
Missing	6	5.8	2,634	4.6	37	29.1
Total	121		72,959		148	

<sup>1</sup>For all respondents to first and second questionnaire ( $N = 73,080$ ).–<sup>2</sup>For all respondents to first questionnaire ( $N = 90,245$ ).–<sup>3</sup>The temporal association between thyroid condition and cancer prior to the first questionnaire is unknown.–<sup>4</sup>Includes only women.

The highest risk estimate working before the age of 20 was for the pre-1960s era, but the opposite was true for holding patients for procedures. Essentially no clear pattern emerged for these 2 variables.

#### Retrospective incident thyroid cancer

One hundred forty eight thyroid cancers were reported as having been diagnosed before completion of the first questionnaire and 2 years postcertification (Table I). As expected, the individuals diagnosed with these cancers began their careers as radiologic technologists much earlier than the prospectively identified cases and, therefore, the analyses of their work history variables differs somewhat from the analyses for the prospective cases. Medical or physician records validated 147 of the 148 reported cases, of these 83 (56.0%) were papillary, 17 (11.5%) were follicular and 2 (1.4%) were medullary, with the rest (31.1%) not classifiable by histology. The retrospectively identified cases were similar to the prospective cases with respect to gender, ethnic group, smoking habit and history of therapeutic X-ray to the head, but were older at baseline and the women reported a later age at menarche.

The associations between work histories of the eligible retrospective incident cases differed slightly from the analysis of pro-

spective incident thyroid cancers. The risk of thyroid cancer was greater for those who first worked before 1950. Among those eligible to work by 1949, the risk increased with duration of pre-1950 employment (Table V). Beginning work as a radiologic technologist before age 18, or age 18–20, was not associated with thyroid cancer risk. Higher potential for exposure, as indicated by not routinely wearing a lead apron when first working as a radiologic technologist, was suggestive of a higher risk for thyroid cancer ( $HR = 1.41$ , 95%  $CI = 0.78$ – $2.57$ ); however, another metric of exposure potential, number of times holding a patient, did not show an association with thyroid cancer.

#### Discussion

In our study of thyroid cancers in radiologic technologists some associations between occupational history and thyroid cancer risk were observed. Only one indicator of occupational exposure to ionizing radiation, whether a technologist held a patient for X-rays, was associated with risk of incident thyroid cancer after the baseline survey. This association, however, was not consistent across eras and specifically not observed for those first employed prior to 1960, when exposures were likely higher. It is also tem-

pered by the lack of an association with other indicators of exposure. The association between occupational exposures in early calendar years and thyroid cancers diagnosed before the baseline survey, specifically a more than 2-fold risk for first employment before 1950 and for working 25 or more years, and a 3-fold risk for working 5 or more years before 1950, are more suggestive of an occupational radiation exposure etiology.

There are some inherent limitations of these data to be considered when evaluating associations between employment as a radiologic technologist and thyroid cancer. The primary limitation of our study is the absence of quantitative exposure data. Self-reported work histories supplied all of the exposure information in this cohort, and while there is considerable heterogeneity in these histories, the actual thyroid doses were not available. However, for the prospective analysis of incident thyroid cancer, occupational history information was obtained from the first questionnaire before diagnosis of thyroid cancer, thus limiting differential recall bias between participants with and without thyroid cancer. Differential recall bias cannot be ruled

out in the analysis of retrospective incident thyroid cancer; however, the exposure metrics used, years employed, are less likely to be subjective. A second potential limitation is that because this cohort was enumerated retrospectively in 1983 with the collection of baseline information on the first questionnaire, prospective ascertainment of risk began many years after first exposure for a substantial part of the cohort. Thus, we were concerned that thyroid cancers occurring before the first questionnaire were relevant, given the higher radiation exposures experienced in earlier eras, the relatively short latency of radiation induced thyroid cancer and the potential early age of onset. The supplemental analysis of retrospective incident thyroid cancer cases assumed that the questionnaire respondents were representative of the target population at risk of developing thyroid cancer in the time before cohort enumeration. It is unknown whether technologists diagnosed with thyroid cancer before 1983 were over or under-represented among participants in the baseline survey. The response rates among technologists known to be alive and for whom an address was available, was 68% for the first survey and 72% for the second survey. While these rates were not ideal, they are respectable for observational studies conducted in the US. Strength of the study is the validation of most of the incident thyroid cancers based on medical records and a very high positive predictive value (91.7%).

The results for nonoccupational risk factors for thyroid cancer were similar in our study compared to previously reported data. The increased risk of thyroid cancer in women was expected based on national thyroid cancer incidence data where women exhibit a 2- to 3-fold risk compared to men.<sup>19</sup> Incidence data show that, unlike most other cancers, thyroid cancer incidence in women peaks at a relatively young age, 35–50. It is noteworthy that the average age of the cohort at the beginning of follow-up in 1983 was relatively young (about 40 years). Thus, the effects of occupational exposures encountered by the youngest cohort members may not be manifest for several more years. In our study, BMI was associated with thyroid cancer risk, which corroborates previously reported associations. A pooled analysis of thyroid cancer studies found an odds ratio of 1.2 for the highest tertile of BMI at diagnosis in women, with no association between BMI and thyroid cancer risk in men.<sup>20</sup> The current analysis found a similar association with a HR of 1.8 for the highest tertile compared to the lowest. A history of smoking was inversely related to thyroid cancer risk. The reason for lower thyroid cancer risk among smokers is unknown, but odds ratios of about 0.5–0.7 have been observed by other investigators.<sup>21–23</sup>

TABLE II – SELECTED OCCUPATIONAL HISTORY CHARACTERISTICS AND THE RISK OF THYROID CANCER IDENTIFIED PROSPECTIVELY AFTER BASELINE AMONG US RADIOLOGIC TECHNOLOGISTS (1983–1998)

	Categories	N	HR <sup>1</sup>	95% CI
Total years worked (tertiles)	<9	52	1.0	
	9–13	35	0.86	0.56–1.33
	>13	34	0.83	0.49–1.40
Year first worked	≥1970	59	1.0	
	1960–1969	42	0.95	0.53–1.70
	<1960	19	0.89	0.30–2.63
Years worked <1960 <sup>2</sup>	0	4	1.0	
	1–5	11	1.85	0.57–5.99
	>5	8	2.17	0.51–9.29
Years worked 1960–1969 <sup>3</sup>	0	24	1.0	
	1–5	31	0.83	0.48–1.44
	>5	23	0.87	0.46–1.64
Years worked ≥1970	0	15	1.0	
	1–5	19	0.81	0.40–1.64
	>5	87	0.78	0.43–1.42
Worked before age 20	No	65	1.0	
	Yes	56	1.02	0.71–1.47

<sup>1</sup>All models adjusted for gender and age at baseline.<sup>2</sup>Includes only technologists born before 1942.<sup>3</sup>Includes only technologists born before 1952.

TABLE III – SELECTED PROCEDURES AND THE RISK OF THYROID CANCER IDENTIFIED PROSPECTIVELY AFTER BASELINE AMONG US RADIOLOGIC TECHNOLOGISTS (1983–1998)

	Categories	N	HR <sup>1</sup>	95% CI
Held Patient for procedures	<50 times	44	1.0	
	≥50 times	71	1.47	1.01–2.15
Had X-rays practiced on self	Never	104	1.0	
	Ever	17	1.46	0.86–2.46
For each year worked with		121		
	Diagnostic procedures <sup>2</sup>		0.98	0.96–1.01
	Therapeutic procedures <sup>3</sup>		0.98	0.91–1.06
Nuclear medicine <sup>4</sup>			1.02	0.96–1.08
Era first worked with				
	Diagnostic procedures <sup>2</sup>			
	≥1970	60	1.0	
	1960–1969	41	1.28	0.69–2.35
Therapeutic procedures <sup>3</sup>				
	<1960	20	1.85	0.71–4.81
	≥1970	98	1.0	
	1960–1969	19	0.87	0.39–1.93
Nuclear medicine <sup>4</sup>				
	<1960	4	0.57	0.16–2.01
	≥1970	98	1.0	
	1960–1969	18	0.97	0.45–2.11
	<1960	5	0.85	0.26–2.71

<sup>1</sup>All models adjusted for gender and age at baseline.<sup>2</sup>Diagnostic procedures included fluoroscopy, dental, routine x-ray, multifilm and CAT scan. Adjusted for era first worked with therapeutic and nuclear procedures, and years worked with all procedures.<sup>3</sup>Therapeutic procedures included orthovoltage, cobalt 60, betatron and other X-ray teletherapy. Adjusted for era first worked with diagnostic and nuclear procedures, and years worked with all procedures.<sup>4</sup>Nuclear procedures included diagnostic radioisotopes, radium therapy and other radioisotope therapy. Adjusted for era first worked with diagnostic and therapeutic procedures, and years worked with all procedures.

**TABLE IV** – SELECTED OCCUPATIONAL HISTORY CHARACTERISTICS BY THE ERA OF FIRST EMPLOYMENT AND THE RISK OF THYROID CANCER IDENTIFIED PROSPECTIVELY AFTER BASELINE AMONG US RADIOLOGIC TECHNOLOGISTS (1983–1998)

	Categories	N	HR <sup>1</sup>	95% CI
First worked <1960				
First worked before age 20	No	8	1.0	
	Yes	11	1.40	0.52–3.72
Held Patient for procedures	<50 times	8	1.0	
	≥50 times	10	0.98	0.39–2.50
First worked 1960–1969				
First worked before age 20	No	18	1.0	
	Yes	24	1.18	0.63–2.20
Held patient for procedures	<50 times	12	1.0	
	≥50 times	30	1.80	0.92–3.53
First worked 1970 or later				
First worked before age 20	No	40	1.0	
	Yes	19	0.83	0.41–1.47
Held patient for procedures	<50 times	25	1.0	
	≥50 times	34	1.49	0.89–2.49

<sup>1</sup>All models adjusted for gender and age at baseline.

**TABLE V** – SELECTED OCCUPATIONAL HISTORY CHARACTERISTICS AND THE RISK OF THYROID CANCER DIAGNOSED AFTER TWO YEARS OF CERTIFICATION AND BEFORE COMPLETION OF A BASELINE SURVEY FOR THE US RADIOLOGIC TECHNOLOGISTS STUDY (N = 90,245)

	Categories	N <sup>1</sup>	HR <sup>2</sup>	95% CI
Total cases		148		
Total years worked <sup>3</sup>	<5	28	1.0	
	5–14	82	0.96	0.62–1.48
	15–24	23	0.96	0.53–1.76
	≥25	12	2.29	0.99–5.32
Year first worked <sup>4</sup>	≥1970	32	1.0	
	1960–1969	51	1.14	0.59–2.19
	1950–1959	36	1.27	0.50–3.20
	1940–1949	20	2.44	0.74–8.06
	<1940	6	3.21	0.64–16.19
Years worked before 1950 <sup>5</sup>	0	21	1.0	
	1–5	15	1.98	0.77–4.33
	>5	11	3.04	1.01–10.78
Age first worked <sup>6</sup>	≥21	60	1.0	
	18–20	79	0.67	0.45–1.00
	<18	6	0.95	0.39–2.35
Used lead apron when first working <sup>6</sup>	Yes	130	1.0	
	No	13	1.41	0.78–2.57
	Unknown	4	1.27	0.40–4.07
Times held Patient <sup>7</sup>	<10	19	1.0	
	10–24	19	1.01	0.53–1.98
	25–49	29	1.34	0.75–2.40
	≥50	77	1.11	0.67–1.85
	Unknown	4	1.21	0.53–1.92

<sup>1</sup>Numbers exclude those missing for the variable. <sup>2</sup>All models adjusted for gender and birth cohort. <sup>3</sup>Adjusted for total years worked. <sup>4</sup>Adjusted for year first worked. <sup>5</sup>Includes only technologists eligible to work by 1949, adjusted for years worked after 1949. <sup>6</sup>Adjusted for year first worked. <sup>7</sup>Adjusted for year first worked.

Radiation to the head and neck area during childhood is known to increase the risk of thyroid cancer, and is seen as soon as 5 years posttreatment and alters the baseline risk for life.<sup>3</sup> Similarly, a history of benign thyroid conditions places individuals in higher thyroid cancer risk categories.<sup>24</sup> These 2 factors are among the most widely reported predictors of thyroid cancer risk, and both were observed in our study. It did not, however, appear that a history of radiotherapy or benign thyroid condition obscured or magnified any association between employment as a radiologic technologist and thyroid cancer risk.

Most of the occupational history covariates did not show an association with prospective incident thyroid cancer risk. The only determinant of occupational radiation exposure that was related to thyroid cancer incidence after the baseline questionnaire was a self-report of holding patients for procedures at least 50 times. This question was asked to ascertain potential exposure based on a work practice; however, 50 times or more was the highest category they could select, and this number could be reached in a relatively short

time if it was a routine or daily practice. All other surrogate measures of occupational radiation exposure in this cohort were not associated with incident thyroid cancer. Although limited to self-reports of work history, it was fairly clear that duration of employment did not influence the risk of thyroid cancer. Although thyroid cancer can be induced by ionizing radiation, these results are not surprising. The risk of radiation-related thyroid cancer has been established for exposures that occur in childhood or adolescence, while exposure to similar doses during adulthood, has not been clearly linked to thyroid cancer.<sup>3–6,25</sup> Given that the occupational radiation exposure was low, fractionated and received during adulthood, the finding of no significant risk elevation was not surprising.

The observed link between early employment as a technologist, especially before 1950, and retrospective incident thyroid cancer diagnosed before completion of the baseline survey are intriguing, and consistent with the likelihood that occupational radiation exposures during that time period were greater than in later years. The possibility of bias in participation and reporting exposures in the cohort members

who had experienced thyroid cancer prior to baseline cannot be ruled out. However, similar associations were observed with breast cancer mortality and nonmelanoma skin cancer in this cohort.<sup>26–28</sup> Because both spontaneous and radiation-related thyroid cancer incidence occurs at a relatively young age, and because the time between radiation exposure and thyroid cancer expression can be short, it is reasonable that many of the radiation-related excess cancers in this cohort occurred before the baseline survey.

Several studies have investigated the thyroid cancer risk for occupations with potential for radiation exposure using broad job classifications compared with the general population. The standardized incidence ratios (SIR) in these studies have been between 1.4 and 2,<sup>9,10,12</sup> which is consistent with the SIR of 1.5 found in the US radiologic technologists cohort.<sup>11</sup> When populations employed in the medical field are compared to an external reference population, it is plausible, given the indolent nature of thyroid cancer, that more frequent screening for thyroid conditions, due to availability of care or recognition of potential hazard based on job history, could account for differences between radiation exposed workers and the general population. In contrast, based on internal comparisons<sup>9</sup> or job histories,<sup>13</sup> radiologic occupations did not have elevated thyroid cancer risk, similar to the generally null findings in our current study based on self-reported work practices.

In summary, our data suggest evidence of a potential occupational etiology of thyroid cancer among subgroups of radiologic technologists who appear to have higher radiation exposures.

Thyroid cancers occurring after completion of a baseline questionnaire in the mid-1980s were generally not associated with employment as a radiologic technologist. This likely reflects the lower occupational exposures of more recent time periods and the possibility that cohort members susceptible to radiogenic thyroid cancer due to higher occupational exposures, experienced in earlier years, had developed thyroid cancer prior to cohort enumeration. Working as a radiologic technologist before 1950 may have resulted in sufficient dose to influence thyroid cancer risk. However, the evidence based on work history data is indirect, and ongoing efforts to estimate historical ionizing radiation exposure and doses experienced by technologists<sup>16</sup> will help clarify these observed associations.

### Acknowledgements

We are grateful to the radiologic technologists who participated in the USRT Study; Mr. Jerry Reid of the American Registry of Radiologic Technologists for continued support of our study; Ms. Diane Kampa of the University of Minnesota for data collection and study coordination; Ms. Kathy Chimes of Westat for tracing and data management and Ms. Jeremy Miller of Information Management Services for biomedical computing. We also extend our appreciation to Drs. John Boice and Jack Mandel who played critical roles in the initiation, design, and follow-up of this cohort study over many years.

### References

- Burgess JR. Temporal trends for thyroid carcinoma in Australia: an increasing incidence of papillary thyroid carcinoma (1982–1997). *Thyroid* 2002;12:141–9.
- Howe HL, Wingo PA, Thun MJ, Ries LA, Rosenberg HM, Feigal EG, Edwards BK. Annual report to the nation on the status of cancer (1973 through 1998), featuring cancers with recent increasing trends. *J Natl Cancer Inst* 2001;93:824–42.
- Inskip PD. Thyroid cancer after radiotherapy for childhood cancer. *Med Pediatr Oncol* 2001;36:568–73.
- Ron E. Thyroid cancer. In: Schottenfeld D, Fraumeni JF, eds. *Cancer epidemiology and prevention*, 2nd edn. Oxford, UK: Oxford University Press, 1996.
- Ron E, Lubin JH, Shore RE, Mabuchi K, Modan B, Pottern LM, Schneider AB, Tucker MA, Boice JD, Jr. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. *Radiat Res* 1995;141:259–77.
- Thompson DE, Mabuchi K, Ron E, Soda M, Tokunaga M, Ochiaiubo S, Sugimoto S, Ikeda T, Terasake M, Izumi S, Preson DL. Cancer incidence in atomic bomb survivors, part 2: solid tumors, 1958–1987. *Radiat Res* 1994;137:S17–S67.
- Cardis E, Kesminiene A, Ivanov V, Malakhova I, Shibata Y, Khrouch V, Drozdovitch V, Maceika E, Zvonova I, Vlassov O, Bouville A, Goulko G et al. Risk of thyroid cancer after exposure to <sup>131</sup>I in childhood. *J Natl Cancer Inst* 2005;97:724–32.
- Farahti J, Demidchik EP, Biko J, Reiners C. Inverse association between age at the time of radiation exposure and extent of disease in cases of radiation-induced childhood thyroid carcinoma in Belarus. *Cancer* 2000;88:1470–6.
- Sont WN, Zielinski JM, Ashmore JP, Jiang H, Krewski D, Fair ME, Band PR, Létourneau EG. First analysis of cancer incidence and occupational radiation exposure based on the national dose registry of Canada. *Am J Epidemiol* 2001;153:309–18.
- Wang JX, Inskip PD, Boice JD, Jr, Li BX, Zhang JY, Fraumeni JF, Jr. Cancer incidence among medical diagnostic X-ray workers in China, 1950 to 1985. *Int J Cancer* 1990;45:889–95.
- Sigurdson AJ, Doody MM, Rao RS, Freedman DM, Alexander BH, Hauptmann M, Mohan AK, Yoshinaga S, Hill DA, Tarone R, Mabuchi K, Ron E et al. Cancer incidence in the US radiologic technologists health study, 1983–1998. *Cancer* 2003;97:3080–9.
- Carstensen JM, Wingren G, Tatschek T, Fredriksson M, Noorlind-Brage H, Axelson O. Occupational risks of thyroid cancer: data from the Swedish Cancer Environment Register, 1961–1979. *Am J Ind Med* 1990;18:535–40.
- Fincham SM, Ugnat A, Hill GB, Kreiger N, Mao Y. Is occupation a risk factor for thyroid cancer? *J Occup Environ Med* 2000;42:318–22.
- Boice JD, Mandel JS, Doody MM, Yoder RC, McGowan R. A health survey of radiologic technologists. *Cancer* 1992;69:586–98.
- Doody MM, Mandel JS, Boice JD. Employment practices and breast cancer among radiologic technologists. *J Occup Environ Med* 1995;37:321–7.
- Simon SL, Weinstock RM, Doody MM, Neaton J, Wenzl T, Stewart P, Mohan AK, Yoder C, Hauptmann M, Freedman M, Cardarelli J, Feng HA et al. Status report on estimating historical radiation doses to a cohort of US radiologic technologists. Spanish Radiation Protection Society, Madrid, 2004. Available at: [www.irpa11.com/new/pdfs/5f39.pdf](http://www.irpa11.com/new/pdfs/5f39.pdf).
- Breslow NE, Day NE. *Statistical methods in cancer research, vol. 2: the design and analysis of cohort studies*. Lyon: International Agency for Research on Cancer, 1987.
- Friedman M. Piecewise exponential models for survival data with covariates. *Ann Stat* 1982;10:101–13.
- Jemal A, Clegg LX, Ward E, Ries LA, Wu X, Jamison PM, Wingo PA, Howe HL, Anderson RN, Edwards BK. Annual report to the nation on the status of cancer, 1975–2001, with a special feature regarding survival. *Cancer* 2004;101:3–27.
- Dal Maso L, La Vecchia C, Franceschi S, Preston-Martin S, Ron E, Levi F, Mack W, Mark SD, McTiernan A, Kolonel L, Mabuchi K, Jin F et al. A pooled analysis of thyroid cancer studies. V. Anthropometric factors. *Cancer Causes Control* 2000;11:137–44.
- Krieger N, Parkes R. Cigarette smoking and the risk of thyroid cancer. *Eur J Cancer* 2000;36:1969–73.
- Mack WJ, Preston-Martin S, Dal Maso L, Galanti R, Xiang M, Franceschi S, Hallquist A, Jin F, Kolonel L, La Vecchia C, Levi F, Linos A et al. A pooled analysis of case-control studies of thyroid cancer: cigarette smoking and consumption of alcohol, coffee, and tea. *Cancer Causes Control* 2003;14:773–85.
- Rossing MA, Cushing KL, Voight LF, Wicklund KG, Daling JR. Risk of papillary thyroid cancer in women in relation to smoking and alcohol consumption. *Epidemiology* 2000;11:49–54.
- Franceschi S, Preston-Martin S, Dal Maso L, Negri E, La Vecchia C, Mack WJ, McTiernan A, Kolonel L, Mark SD, Mabuchi K, Jin F, Wingren G et al. A pooled analysis of case-control studies of thyroid cancer. IV. Benign thyroid diseases. *Cancer Causes Control* 1999;10:583–95.
- Ron E. Ionizing radiation and cancer risk: evidence from epidemiology. *Radiat Res* 1998;150(5, Suppl):S30–41.
- Mohan AK, Hauptmann M, Linet MS, Ron E, Lubin JH, Freedman DM, Alexander BH, Boice JD, Doody MM, Matanoski GM. Breast cancer mortality among radiologic technologists in the United States. *J Natl Cancer Inst* 2002;94:943–8.
- Yoshinaga S, Hauptmann M, Sigurdson AJ, Doody MM, Freedman DM, Alexander BH, Linet MS, Ron E, Mabuchi K. Non-melanoma skin cancer in relation to ionizing radiation exposure among US radiologic technologists. *Int J Cancer* 2005;115:828–34.
- Doody MM, Freedman DM, Alexander BH, Hauptmann M, Hill DA, Tarone R, Rao RS, Mabuchi K, Ron E, Sigurdson AJ, Linet MS. Breast cancer incidence in US radiologic technologists. *Cancer*, in press.